

4



SEQUENCE LISTING

<110> Chambers, Thomas J.
Guirakhoo, Farshad
Monath, Thomas P.

<120> CHIMERIC FLAVIVIRUS VACCINES

<130> 06132/033003

<140> 09/121,587

<141> 1998-07-23

<150> 08/807,445

<151> 1997-02-28

<150> 09/007,664

<151> 1998-01-15

<160> 20

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 21

<212> DNA

<213> Artificial Sequence

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<223> Derived from Yellow Fever virus and West Nile
virus

<400> 1

cactgggaga gcttgaaggt c

21

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virus

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aaagccagtt gcagccgcgg tttaa

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<210> 3

<211> 21

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 <400> 3
 aaggtagact ggtgggctcc c 21

 <210> 4
 <211> 26
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 <213> Artificial Sequence

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 <223> Derived from Yellow Fever virus and Dengue-1 virus

 <400> 4
 gatcctcagt accaaccgcg gtttaa 26

 <210> 5
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 <223> Derived from Yellow Fever virus and Dengue-2 virus

 <400> 5
 aaggtagatt ggtgtgcatt g 21

 <210> 6
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 <220>
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 <400> 6
 aaccctcagt accaccgcg gtttaa 26

 <210> 7
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 <223> Derived from Yellow Fever virus and Dengue-3 virus

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aaggtgaatt gaagtgtct a 21

<210> 8

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<400> 8

acccccagca ccaccgcgg tttaa 25

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<211> 21

<212> DNA

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<223> Derived from Yellow Fever virus and Dengue-4 virus

<400> 9

aaaaggaaca gttgttctct a 21

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<211> 25

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<223> Derived from Yellow Fever virus and Dengue-4 virus

<400> 10

accggaagtg tcaaccgcgg tttaa 25

<210> 11

<211> 21

<212> DNA

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<223> Derived from Yellow Fever virus and St. Louis
Encephalitis virus

<400> 11

aacgtgaata gttgatagt c 21

<210> 12

<211> 25

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 <223> Derived from Yellow Fever virus and St. Louis
 Encephalitis virus

<400> 12
 accgttggtc gcacccgcgg tttaa 25

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 Encephalitis virus

<400> 13
 aatttcgaaa ggtggaaggt c 21

<210> 14
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 <212> DNA
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<220>
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 Encephalitis virus

<400> 14
 gaccggtggt tacagccgcg gtttaa 26

<210> 15
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<220>
 <223> Derived from Yellow Fever virus and Tick-Borne
 Encephalitis virus

<400> 15
 tactgcgaac gacgttgcca c 21

<210> 16
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<220>
 <223> Derived from Yellow Fever virus and Tick-Borne
 Encephalitis virus

<400> 16
actgggaacc tcacccgcgg tttaa

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<210> 17
<211> 1983
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<213> Dengue-2 virus

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<222> (1)...(1983)

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1 5 10 15
caa gag aaa ggg aaa agt ctt ttg ttt aaa aca gag gat ggc gtg aac 96
Gln Glu Lys Gly Lys Ser Leu Leu Phe Lys Thr Glu Asp Gly Val Asn
20 25 30
atg tgc acc ctc atg gcc atg gac ctt ggt gaa ttg tgt gaa gac aca 144
Met Cys Thr Leu Met Ala Met Asp Leu Gly Glu Leu Cys Glu Asp Thr
35 40 45
atc acg tac aag tgt ccc ctt ctc agg cag aat gag cca gaa gac ata 192
Ile Thr Tyr Lys Cys Pro Leu Leu Arg Gln Asn Glu Pro Glu Asp Ile
50 55 60
gac tgc tgg tgc aac tcc acg tcc acg tgg gta acc tat ggg act tgt 240
Asp Cys Trp Cys Asn Ser Thr Ser Thr Trp Val Thr Tyr Gly Thr Cys
65 70 75 80
acc acc acg gga gaa cat aga aga gaa aaa aga tca gtg gca ctc gtt 288
Thr Thr Thr Gly Glu His Arg Arg Glu Lys Arg Ser Val Ala Leu Val
85 90 95
cca cat gtg gga atg gga ctg gag acg cga act gaa aca tgg atg tca 336
Pro His Val Gly Met Gly Leu Glu Thr Arg Thr Glu Thr Trp Met Ser
100 105 110
tca gaa ggg gct tgg aaa cat gcc cag aga att gaa att tgg atc ctg 384
Ser Glu Gly Ala Trp Lys His Ala Gln Arg Ile Glu Ile Trp Ile Leu
115 120 125
aga cat cca ggc ttc acc ata atg gca gca atc ctg gca tac acc ata 432
Arg His Pro Gly Phe Thr Ile Met Ala Ala Ile Leu Ala Tyr Thr Ile
130 135 140
ggg acg aca cat ttc cag aga gca ctg att ttc atc tta ctg aca gct 480
Gly Thr Thr His Phe Gln Arg Ala Leu Ile Phe Ile Leu Leu Thr Ala

145	150	155	160	
gtc gct cct tca atg aca atg cgt tgc ata gga ata tca aat aga gac				528
Val Ala Pro Ser Met Thr Met Arg Cys Ile Gly Ile Ser Asn Arg Asp				
	165	170	175	
ttt gta gaa ggg gtt tca gga gga agc tgg gtt gac ata gtc tta gaa				576
Phe Val Glu Gly Val Ser Gly Gly Ser Trp Val Asp Ile Val Leu Glu				
	180	185	190	
cat gga agc tgt gtg acg acg atg gca aaa aac aaa cca aca ttg gat				624
His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr Leu Asp				
	195	200	205	
ttt gaa ctg ata aaa aca gaa gcc aaa cag cct gcc acc cta agg aag				672
Phe Glu Leu Ile Lys Thr Glu Ala Lys Gln Pro Ala Thr Leu Arg Lys				
	210	215	220	
tac tgt ata gag gca aag cta acc aac aca aca aca gaa tct cgt tgc				720
Tyr Cys Ile Glu Ala Lys Leu Thr Asn Thr Thr Thr Glu Ser Arg Cys				
	225	230	235	240
cca aca caa ggg gaa ccc agc cta aat gaa gag cag gat aaa agg ttc				768
Pro Thr Gln Gly Glu Pro Ser Leu Asn Glu Glu Gln Asp Lys Arg Phe				
	245	250	255	
gtc tgc aaa cac tcc atg gta gac aga gga tgg gga aat gga tgt gga				816
Val Cys Lys His Ser Met Val Asp Arg Gly Trp Gly Asn Gly Cys Gly				
	260	265	270	
tta ttt gga aag gga ggc att gtg acc tgt gct atg ttc aca tgc aaa				864
Leu Phe Gly Lys Gly Gly Ile Val Thr Cys Ala Met Phe Thr Cys Lys				
	275	280	285	
aag aac atg gag gga aaa gtt gtg cag cca gaa aac ttg gaa tac acc				912
Lys Asn Met Glu Gly Lys Val Val Gln Pro Glu Asn Leu Glu Tyr Thr				
	290	295	300	
att gtg gta aca ccc cac tca ggg gaa gag cat gcg gtc gga aat gac				960
Ile Val Val Thr Pro His Ser Gly Glu Glu His Ala Val Gly Asn Asp				
	305	310	315	320
aca gga aaa cat ggc aag gaa atc aaa gta aca cca cag agt tcc atc				1008
Thr Gly Lys His Gly Lys Glu Ile Lys Val Thr Pro Gln Ser Ser Ile				
	325	330	335	
aca gaa gca gaa ttg aca ggt tat ggc act gtc acg atg gag tgc tct				1056
Thr Glu Ala Glu Leu Thr Gly Tyr Gly Thr Val Thr Met Glu Cys Ser				
	340	345	350	
ccg aga aca ggc ctc gac ttc aat gag atg gtg ttg ctg cag atg gaa				1104

Pro	Arg	Thr	Gly	Leu	Asp	Phe	Asn	Glu	Met	Val	Leu	Leu	Gln	Met	Glu		
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aat	aaa	gct	tgg	ctg	gtg	cat	agg	caa	tgg	ttc	cta	gac	ctg	ccg	tta	1152	
Asn	Lys	Ala	Trp	Leu	Val	His	Arg	Gln	Trp	Phe	Leu	Asp	Leu	Pro	Leu		
	370					375				380							
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Pro	Trp	Leu	Pro	Gly	Ala	Asp	Thr	Gln	Gly	Ser	Asn	Trp	Ile	Gln	Lys		
385				390					395						400		
gaa	aca	ttg	gtc	act	ttc	aaa	aat	cct	cat	gcg	aag	aaa	cag	gat	gtt	1248	
Glu	Thr	Leu	Val	Thr	Phe	Lys	Asn	Pro	His	Ala	Lys	Lys	Gln	Asp	Val		
			405					410					415				
gtt	gtt	tta	gga	tcc	caa	gaa	ggg	gcc	atg	cac	aca	gca	ctc	aca	ggg	1296	
Val	Val	Leu	Gly	Ser	Gln	Glu	Gly	Ala	Met	His	Thr	Ala	Leu	Thr	Gly		
		420					425					430					
gcc	aca	gaa	atc	caa	atg	tca	tca	gga	aac	tta	ctc	ttc	aca	gga	cat	1344	
Ala	Thr	Glu	Ile	Gln	Met	Ser	Ser	Gly	Asn	Leu	Leu	Phe	Thr	Gly	His		
	435					440						445					
ctc	aag	tgc	agg	ctg	aga	atg	gac	aag	cta	cag	ctc	aaa	gga	atg	tca	1392	
Leu	Lys	Cys	Arg	Leu	Arg	Met	Asp	Lys	Leu	Gln	Leu	Lys	Gly	Met	Ser		
	450					455					460						
tac	tct	atg	tgc	aca	gga	aag	ttt	aaa	gtt	gtg	aag	gaa	ata	gca	gaa	1440	
Tyr	Ser	Met	Cys	Thr	Gly	Lys	Phe	Lys	Val	Val	Lys	Glu	Ile	Ala	Glu		
465				470					475						480		
aca	caa	cat	gga	aca	ata	gtt	atc	agg	gtg	cag	tat	gaa	ggg	gac	ggc	1488	
Thr	Gln	His	Gly	Thr	Ile	Val	Ile	Arg	Val	Gln	Tyr	Glu	Gly	Asp	Gly		
			485					490						495			
tct	cca	tgt	aaa	atc	cct	ttt	gag	ata	atg	gat	ttg	gaa	aaa	aga	cat	1536	
Ser	Pro	Cys	Lys	Ile	Pro	Phe	Glu	Ile	Met	Asp	Leu	Glu	Lys	Arg	His		
		500					505					510					
gtc	tta	ggt	cgc	ctg	atc	aca	gtc	aac	cca	att	gtg	aca	gaa	aaa	gat	1584	
Val	Leu	Gly	Arg	Leu	Ile	Thr	Val	Asn	Pro	Ile	Val	Thr	Glu	Lys	Asp		
		515					520					525					
agc	cca	gtc	aac	ata	gaa	gca	gaa	cct	cca	ttc	gga	gac	agc	tac	atc	1632	
Ser	Pro	Val	Asn	Ile	Glu	Ala	Glu	Pro	Pro	Phe	Gly	Asp	Ser	Tyr	Ile		
	530					535					540						
atc	ata	gga	gta	gag	ccg	gga	caa	ctg	aag	ctc	aac	tgg	ttt	aag	aaa	1680	
Ile	Ile	Gly	Val	Glu	Pro	Gly	Gln	Leu	Lys	Leu	Asn	Trp	Phe	Lys	Lys		
545				550					555						560		

gga agt tct atc ggc caa atg ttt gag aca aca atg agg ggg gcg aag 1728
 Gly Ser Ser Ile Gly Gln Met Phe Glu Thr Thr Met Arg Gly Ala Lys
 565 570 575

aga atg gcc att ttg ggt gac aca gcc tgg gat ttt gga tcc ctg gga 1776
 Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser Leu Gly
 580 585 590

gga gtg ttt aca tct ata gga aaa gcc ctc cac caa gtc ttt gga gca 1824
 Gly Val Phe Thr Ser Ile Gly Lys Ala Leu His Gln Val Phe Gly Ala
 595 600 605

atc tat gga gct gcc ttc agt ggg gtc tca tgg act atg aaa atc ctc 1872
 Ile Tyr Gly Ala Ala Phe Ser Gly Val Ser Trp Thr Met Lys Ile Leu
 610 615 620

ata gga gtc att atc aca tgg ata gga atg aat tca cgc agc acc tca 1920
 Ile Gly Val Ile Ile Thr Trp Ile Gly Met Asn Ser Arg Ser Thr Ser
 625 630 635 640

ctg tct gtg tca cta gta ttg gtg gga gtc gtg acg ctg tat ttg gga 1968
 Leu Ser Val Ser Leu Val Leu Val Gly Val Val Thr Leu Tyr Leu Gly
 645 650 655

gtt atg gtg ggc gcc 1983
 Val Met Val Gly Ala
 660

<210> 18
 <211> 661
 <212> PRT
 <213> Dengue-2 virus

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 Phe His Leu Thr Thr Arg Asn Gly Glu Pro His Met Ile Val Ser Arg
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 Gln Glu Lys Gly Lys Ser Leu Leu Phe Lys Thr Glu Asp Gly Val Asn
 20 25 30
 Met Cys Thr Leu Met Ala Met Asp Leu Gly Glu Leu Cys Glu Asp Thr
 35 40 45
 Ile Thr Tyr Lys Cys Pro Leu Arg Gln Asn Glu Pro Glu Asp Ile
 50 55 60
 Asp Cys Trp Cys Asn Ser Thr Ser Thr Trp Val Thr Tyr Gly Thr Cys
 65 70 75 80
 Thr Thr Thr Gly Glu His Arg Arg Glu Lys Arg Ser Val Ala Leu Val
 85 90 95
 Pro His Val Gly Met Gly Leu Glu Thr Arg Thr Glu Thr Trp Met Ser
 100 105 110
 Ser Glu Gly Ala Trp Lys His Ala Gln Arg Ile Glu Ile Trp Ile Leu
 115 120 125

Arg	His	Pro	Gly	Phe	Thr	Ile	Met	Ala	Ala	Ile	Leu	Ala	Tyr	Thr	Ile
130						135					140				
Gly	Thr	Thr	His	Phe	Gln	Arg	Ala	Leu	Ile	Phe	Ile	Leu	Leu	Thr	Ala
145					150					155					160
Val	Ala	Pro	Ser	Met	Thr	Met	Arg	Cys	Ile	Gly	Ile	Ser	Asn	Arg	Asp
				165					170					175	
Phe	Val	Glu	Gly	Val	Ser	Gly	Gly	Ser	Trp	Val	Asp	Ile	Val	Leu	Glu
			180					185					190		
His	Gly	Ser	Cys	Val	Thr	Thr	Met	Ala	Lys	Asn	Lys	Pro	Thr	Leu	Asp
		195					200					205			
Phe	Glu	Leu	Ile	Lys	Thr	Glu	Ala	Lys	Gln	Pro	Ala	Thr	Leu	Arg	Lys
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Tyr	Cys	Ile	Glu	Ala	Lys	Leu	Thr	Asn	Thr	Thr	Thr	Glu	Ser	Arg	Cys
225					230					235					240
Pro	Thr	Gln	Gly	Glu	Pro	Ser	Leu	Asn	Glu	Glu	Gln	Asp	Lys	Arg	Phe
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Val	Cys	Lys	His	Ser	Met	Val	Asp	Arg	Gly	Trp	Gly	Asn	Gly	Cys	Gly
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Leu	Phe	Gly	Lys	Gly	Gly	Ile	Val	Thr	Cys	Ala	Met	Phe	Thr	Cys	Lys
		275					280					285			
Lys	Asn	Met	Glu	Gly	Lys	Val	Val	Gln	Pro	Glu	Asn	Leu	Glu	Tyr	Thr
	290					295					300				
Ile	Val	Val	Thr	Pro	His	Ser	Gly	Glu	Glu	His	Ala	Val	Gly	Asn	Asp
305					310					315					320
Thr	Gly	Lys	His	Gly	Lys	Glu	Ile	Lys	Val	Thr	Pro	Gln	Ser	Ser	Ile
			325						330					335	
Thr	Glu	Ala	Glu	Leu	Thr	Gly	Tyr	Gly	Thr	Val	Thr	Met	Glu	Cys	Ser
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Pro	Arg	Thr	Gly	Leu	Asp	Phe	Asn	Glu	Met	Val	Leu	Leu	Gln	Met	Glu
		355					360					365			
Asn	Lys	Ala	Trp	Leu	Val	His	Arg	Gln	Trp	Phe	Leu	Asp	Leu	Pro	Leu
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Glu	Thr	Leu	Val	Thr	Phe	Lys	Asn	Pro	His	Ala	Lys	Lys	Gln	Asp	Val
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Val	Val	Leu	Gly	Ser	Gln	Glu	Gly	Ala	Met	His	Thr	Ala	Leu	Thr	Gly
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Leu	Lys	Cys	Arg	Leu	Arg	Met	Asp	Lys	Leu	Gln	Leu	Lys	Gly	Met	Ser
	450					455					460				
Tyr	Ser	Met	Cys	Thr	Gly	Lys	Phe	Lys	Val	Val	Lys	Glu	Ile	Ala	Glu
465					470					475					480
Thr	Gln	His	Gly	Thr	Ile	Val	Ile	Arg	Val	Gln	Tyr	Glu	Gly	Asp	Gly
			485						490					495	
Ser	Pro	Cys	Lys	Ile	Pro	Phe	Glu	Ile	Met	Asp	Leu	Glu	Lys	Arg	His
		500						505					510		
Val	Leu	Gly	Arg	Leu	Ile	Thr	Val	Asn	Pro	Ile	Val	Thr	Glu	Lys	Asp
	515						520					525			
Ser	Pro	Val	Asn	Ile	Glu	Ala	Glu	Pro	Pro	Phe	Gly	Asp	Ser	Tyr	Ile

530		535		540	
Ile Ile Gly Val Glu Pro Gly Gln Leu Lys Leu Asn Trp Phe Lys Lys					
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Gly Ser Ser Ile Gly Gln Met Phe Glu Thr Thr Met Arg Gly Ala Lys					
	565		570		575
Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser Leu Gly					
	580		585		590
Gly Val Phe Thr Ser Ile Gly Lys Ala Leu His Gln Val Phe Gly Ala					
	595		600		605
Ile Tyr Gly Ala Ala Phe Ser Gly Val Ser Trp Thr Met Lys Ile Leu					
	610		615		620
Ile Gly Val Ile Ile Thr Trp Ile Gly Met Asn Ser Arg Ser Thr Ser					
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Leu Ser Val Ser Leu Val Leu Val Gly Val Val Thr Leu Tyr Leu Gly					
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<210> 19

<211> 11916

<212> DNA

<213> Artificial Sequence

<220>

<223> Derived from Yellow Fever virus and Japanese Encephalitis virus

<400> 19

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gtctgggtcgt	aaagctcagg	gaaaaaccct	gggcgtcaat	atggtagcag	gaggagttcg	180
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<211> 3280

<212> PRT

<213> Artificial Sequence

<220>

<223> Derived from Yellow Fever virus and Japanese
Encephalitis virus

<400> 20

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 85             90             95
Cys Cys Ile Phe Arg Arg Arg Glu Glu Glu Glu Leu Thr His His
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Arg	Glu	Ser	Ser	Ser	Ser	Ser	Ser	Ala	Ala	Asp	Gly	Ile	Ile	His	Ile
			580					585					590		
Ile	Glu	Thr	Leu	Leu	Asp	Trp	Leu	Leu	Gln	Val	Val	Val	Val	Val	Ile
			595				600					605			
Leu	Ser	Ser	Lys	Ile	Ile	Val	Lys	Leu	Leu	Ile	Asn	Ser	Ser	Lys	Pro
	610					615					620				
Pro	Phe	Glu	Glu	Glu	Glu	Glu	Glu	Lys	Cys	Cys	Pro	Lys	Phe	Phe	Leu
625					630					635					640
Thr	Pro	Pro	Glu	His	His	Asp	Val	Glu	Glu	Ala	Gly	Gln	Gln	Gln	Gln
				645					650					655	
Met	Arg	Ser	Ser	Ala	Ile	Phe	Phe	Gly	Lys	Lys	Arg	Trp	Thr	Thr	Ser
			660					665					670		
Val	Val	Val	Ala	Gly	Gly	Gly	Gly	Gly	Lys	Glu	Cys	Cys	Thr	Arg	Arg
			675				680					685			
Gly	Thr	His	His	Ile	Phe	Gln	Gln	Phe	Gly	Gly	Gly	Leu	Gln	Gln	Gln
	690					695					700				
Gln	Gln	Gly	Trp	Trp	Asp	Leu	Gly	Gly	Arg	Thr	Leu	Leu	Phe	Ser	Ser
705					710					715					720
Arg	Glu	Glu	Glu	Met	Glu	Ala	Ala	Ala	Ala	Ser	Ser	Gly	Lys	Ser	Ser
				725					730					735	
Glu	Arg	Arg	Ala	Arg	Phe	Phe	Asn	Arg	Val	Val	Glu	Phe	Phe	Phe	Phe
			740					745					750		
Phe	Pro	Asp	Arg	Arg	Ser	Leu	Leu	Thr	Gly	Val	Val	His	His	Thr	Thr
		755					760					765			
Cys	Thr	Thr	Asp	Ala	Val	Val	Val	Val	Val	Glu	Tyr	Tyr	His	Arg	Leu
	770					775					780				
Leu	Met	Asp	Leu	Leu	Leu	Gly	Gly	Ser	Gly	Glu	Glu	Glu	Lys	Arg	Arg
785					790					795					800
Arg	Arg	Val	Pro	Met	Met	Ser	Pro	Thr	Thr	Leu	Asp	Asp	Glu	Val	Met
				805					810					815	
Met	Val	Asn	Gly	Met	Asp	Asp	Asp	Asp	Asp	Pro	His	Leu	Leu	Arg	
			820				825					830			
His	His	Asp	Tyr	Lys	Lys	Val	Val	Val	His	His	Thr	Ile	Ile	Ile	Ile
		835					840					845			
Ile	Thr	Ser	Ser	Arg	Glu	Glu	Lys	Cys	Ser	Ser	Pro	Arg	Arg	Asn	Arg
	850					855					860				
Arg	Arg	Gln	Leu	Ala	Ala	Ala	Ala	Leu	Thr	Ile	Ile	Ile	Pro	Gly	Gly
865					870					875					880
Gln	Gly	Gly	Arg	Arg	Thr	Thr	Pro	Trp	Met	Met	Gly	Thr	Thr	Thr	Thr
				885					890					895	
Thr	Arg	Ser	Glu	Glu	Lys	Lys	Cys	Pro	Gly	Gly	Arg	Asp	Asp	Leu	
			900				905					910			
Met	Met	Asn	Cys	Asp	Asp	Asp	Asp	Asp	Arg	Gly	Gly	Ile	Asn	Gln	Gln
		915					920					925			
Pro	Pro	Arg	Arg	Ser	Gly	Gly	Ser	Tyr	Ser	Ser	Asn	Gly	Val	Val	Val

930		935		940
Val Ala Ala Pro Pro Thr Met Pro Pro Cys Glu Glu Ser Met Val Val				
945		950		955
Asp Gly Cys Cys Val Ser Ser Ser Ser Ser Gly Asn Gln Gly Gly Thr				960
		965		970
His Glu Glu Pro Ser Gly Gly Ala Pro Pro Val Thr Ala Ala Ala Ala				975
		980		985
Ala Glu Ile Ile Cys Cys Pro Pro Leu Val Trp Trp Ser Met Met Asp				990
		995		1000
Ser Asn Asn Lys Trp Ser Ser Ser Ser Gly Lys Lys Gln Gly Pro Pro				1005
		1010		1015
Ala Asn Asn Trp Leu Glu Glu Val Val Leu Leu Gly Ser Ser Ser Ser				1020
1025		1030		1035
Ser Ala Gly Arg Arg Lys Leu Leu Asp Asp Ala Glu Thr Thr Gln Trp				1040
		1045		1050
Trp Val Gly Leu Leu Leu Leu Leu Phe His His Asp Glu Gln Gln Glu				1055
		1060		1065
Glu Thr Thr Met Tyr Tyr Gly Val Asp Asp Leu Pro Phe Phe Phe Phe				1070
		1075		1080
Gln Ser Asp Asp Gly Leu Leu Leu Arg Leu Leu Gly Ser Gly Gly Leu				1085
		1090		1095
Trp Ser Ser Ser Gly Gly Gly Gly Gly Pro Cys Ala Ala Pro Ala Ala				1100
1105		1110		1115
Met Met Gly Asp Cys Cys Trp Val Val Val Met Gly Gly Gly Gly Gly				1120
		1125		1130
Leu Trp Trp Val Ser Lys Lys Gln Phe Leu Leu Cys Ile Ile Asp Asn				1135
		1140		1145
Lys Lys Leu Leu Leu Leu Leu Leu Gly Lys Lys Ser Asn Thr Thr				1150
		1155		1160
Leu Ala Ala Ser Trp Leu Leu Thr Pro Pro His Tyr Tyr Tyr Tyr				1165
		1170		1175
Tyr Gly Glu Glu Leu Pro Pro Met Phe Phe Phe Cys His Gly Gly Ser				1180
1185		1190		1195
Val Leu His His His His His Asn Phe Phe Gly His Leu Leu Cys Arg				1200
		1205		1210
Arg Arg Ile Pro Pro Gly Gly Pro Pro His Ser His His His His Leu				1215
		1220		1225
Thr Trp Trp Leu Thr Gln Gln Phe Phe Phe Ala Cys Val Val Phe Leu				1230
		1235		1240
Ala Ala Pro His His His His His Trp Ala Lys Lys Val Ser Ser Val				1245
		1250		1255
Asn Glu Glu Thr Arg Ser Ser Leu Val Val Val Gly Val Val Val Val				1260
1265		1270		1275
Val Ala Gly Gly Gly Phe Ser Ser Arg Trp Arg Arg Phe Leu Leu Ser				1280
		1285		1290
Asp Cys Cys Leu Glu Asp Asp Asp Asp Ser Leu Val Ser Ser Gly Trp				1295
		1300		1305
Trp Gly Trp Met Met Leu Glu Leu Leu Glu Ala Ala Ala Ala Ser				1310
		1315		1320
Phe Phe Gly Lys Lys Glu Ala Glu Glu Gln Arg Glu Glu Pro Pro Pro				1325
		1330		1335
				1340

Tyr Asp Val Val Val Val Val Leu Ser Ser Thr Arg Gly Gly Ser Ser
1345 1350 1355 136
Cys Cys Ser Glu Glu Glu Ser Ala Ala Gly Thr Arg Arg Arg Arg Leu
1365 1370 1375
Ser Leu Ala Ala Gly Trp Trp Leu Pro Ser Ser Pro Phe Ala Ala Ser
1380 1385 1390
Ala Ala Ala Ala Ala Pro Cys Trp Trp Gly Cys Cys His Val Arg Arg
1395 1400 1405
Ser Glu Glu Val Gly Gly Val Leu Trp Trp Trp Trp Trp Ile Pro Pro
1410 1415 1420
Ser Asp Asp Ser Arg Asn Asn Glu His His Gly Gly Trp Trp Phe Met
1425 1430 1435 144
Ala Ala Ala Ala Tyr Ser Ser Ser Thr Phe Leu Leu Gly Leu Leu Ser
1445 1450 1455
Glu Glu Glu Gly Val Ala Ala Gly Arg Arg Arg Arg Arg Val Pro His
1460 1465 1470
His Cys Gly Gly Val Thr Arg Arg Ser Phe Pro Pro Ser Gly Gly Gly
1475 1480 1485
Lys Lys Lys Lys Lys Lys Ile Pro Pro Leu Gly Phe Phe Arg Lys Lys
1490 1495 1500
Leu Val Val Leu Trp Trp Trp His Gly Ser Ser Ser Ser Trp Lys Ala
1505 1510 1515 152
Ala Trp Asp Gly Gly Gly Arg Arg Ser Ser Ala Ala Val Val Arg Lys
1525 1530 1535
Lys Lys Lys Lys Arg Gly Gln Gln Ser Arg Arg Lys Pro Ser Ser Val
1540 1545 1550
Gln Ser Ser Gly Met Met Gly Glu Ile Ile Ile Ile Ala Val Val
1555 1560 1565
Ser Leu Leu Arg Val Ala Ala Ser Gly Gly Ser Tyr Cys Cys Thr Gly
1570 1575 1580
Thr Thr Thr Thr Glu Arg Gly Leu Tyr Tyr Gln Trp Trp Ser Leu Ser
1585 1590 1595 160
Ser Asp Asn Ser Ser Arg Val Val Val Val His Ile Pro Pro Leu
1605 1610 1615
Arg Arg Lys Glu Glu Lys Gly Gly Ser Lys Lys Ile Pro Thr
1620 1625 1630
Thr Thr Thr Thr Leu Lys Lys Arg Asn Asp Asp Leu Ser Leu Leu Phe
1635 1640 1645
His His Trp Ser Trp Trp Arg Gln Asp Asp Asp Asp Val Ser Ser Ser
1650 1655 1660
Gln Ile Leu Leu Arg Val Val His Gly Asp Asp Leu Arg Thr Thr Cys
1665 1670 1675 168
Val Val Val Val Val Pro His Gln Gln Leu Phe Phe Ser Glu Met Met
1685 1690 1695
Gly Gly Phe Phe Thr Ala Ala Asp Val Lys Lys Lys Lys Lys His Thr
1700 1705 1710
Thr Gly Phe Phe Phe Leu Thr Ala Ala Gly Arg Arg Ser His Pro Cys
1715 1720 1725
Ala Ala Ala Ala Met Pro Pro Pro Thr Tyr Arg Arg Val Gly Gly Gln
1730 1735 1740
Leu Gly Gly Val Asn Trp Trp Ser Asp Asp Asp Asp Asp Tyr Gly Pro

1745		1750		1755		176
Ile Ile Leu Asp	Pro Pro His Ser Ser	Leu Glu Glu Trp	Ala Ala Ala			
	1765		1770		1775	
Ala Ala Ala Arg	Ala Ala Gly Lys Val	Gln Gln Gln Leu	Met Met Ser			
	1780		1785		1790	
His Thr Thr Leu	Gly Leu Leu Leu Leu	Val Met Asn Asn	Pro His Ser			
	1795		1800		1805	
Ser Trp Lys Met	Met Gln Thr Asp Asp	Thr Gln Gln Gln	Gln Gln Ala			
	1810		1815		1820	
Leu Glu Glu Gln	Gly Gly Asp Trp Ile	Ile Gly Gln Gln	Gly Pro Pro			
	1825		1830		1835	
Ala Trp Phe Phe	Phe Phe Phe Pro	Ser Ser Gln Ser	Cys Cys Met	Ser		
	1845		1850		1855	
Trp Trp Ala Ser	Ser Ala Gly Gly	Glu Arg Val Val	Val Val Trp	Trp		
	1860		1865		1870	
Ser Ser Asn Arg	Lys Lys Leu Glu	Asn Thr Thr Thr	Ile Lys Lys	Glu		
	1875		1880		1885	
Glu Glu Glu Glu	Glu Leu Tyr Tyr	Trp Pro Pro Asp	Ile Ala Ala	Asn		
	1890		1895		1900	
Gly Ser Ser Thr	Phe Phe Val Glu	Arg Arg Arg Arg	Arg Arg Leu	Asp Asp		
	1905		1910		1915	
Gln Asp Gly Gly	Leu Ser Leu Leu	Leu Val Val Arg	Glu Glu Arg	Trp		
	1925		1930		1935	
Gln Gln Gln Gln	Lys Gly Gly Leu	Arg Ile Ile Arg	Ile Ile Leu	Leu		
	1940		1945		1950	
Leu Leu Arg Arg	Gly Gly His Trp	Trp Trp Trp Trp	Lys Ser Gln	Gln		
	1955		1960		1965	
Glu Met Met Asp	Ser Tyr Tyr Leu	Phe Leu Gln Gln	Glu Asn Asn	Asn		
	1970		1975		1980	
Asn Asn Asn His	His His His Leu	Leu Val Val Arg	Pro Gln Gln	Leu Leu		
	1985		1990		1995	
Leu Gln His Gly	Gly Gly Gly Val	Val Val Val Val	Glu Trp Ser	Ser Pro Leu		
	2005		2010		2015	
Tyr Tyr Arg Glu	Leu Lys Lys Pro	Val Ser Ser Trp	Glu Thr Glu	Glu		
	2020		2025		2030	
Met Thr Thr Arg	Lys Val Val Gln	Arg Thr Thr Gly	Gly Cys Asp	Leu		
	2035		2040		2045	
Leu Leu Leu Leu	Val Trp Trp Phe	Val Ala Ala Trp	Pro Arg Arg	Gly		
	2050		2055		2060	
Leu Leu Asp Glu	Val Ser Gly Gly	Gly Gly Val Leu	Lys Lys Pro	Glu		
	2065		2070		2075	
Glu Glu Asp Asp	Met Thr Thr Gly	Glu Thr Thr Glu	Val Val Val	Val		
	2085		2090		2095	
Val Gly Ser Trp	Trp Glu Gln Gln	Lys Pro Leu Leu	Pro Lys Val	Val		
	2100		2105		2110	
Val Met Met Arg	Val Ser Ser Ser	Ser Ser Asp Gln	Gln Cys Ala	Val		
	2115		2120		2125	
Val Asn Leu Leu	Leu Phe Ala Ala	Arg Glu Glu Glu	Leu Leu Leu	Leu		
	2130		2135		2140	
Leu Lys Cys Val	Leu Ser Thr Pro	Pro Ile Ser Trp	Trp Lys Lys			
	2145		2150		2155	
					216	

Gly Gly Arg Gly Gly Gly Gly Gly Gly Tyr His His Val Cys Cys Leu	2165	2170	2175
His Ser Ser Gly Arg Leu Leu Gly Leu Leu Arg Asn Ala Ala Ala Ala	2180	2185	2190
Ala Ser Met Met Ala Gly Gly Gln Met Leu Leu Tyr Thr Gly Gly Asp	2195	2200	2205
Tyr His Arg Glu Glu Val Ile Phe Phe His Val Val Pro Lys Ala Ala	2210	2215	2220
Ser Arg Met Met Tyr Gly Gly Gly Gly Gly Gly His Asn Asn Pro Ala	2225	2230	2235
Ala Gly Tyr Leu Leu Val Pro Trp Trp Ala Ser Ser Pro Thr His His	2245	2250	2255
His His His Ser Tyr Tyr His Ala His His Ser Leu Ser Ser Met Val	2260	2265	2270
Val Cys Asp Pro Pro Ser Gln Gly Gly Gly Gly Asn Lys Gly Gly Ile	2275	2280	2285
Gln Asp Asp Pro Ser Ser His Thr Ser Ser Ile Gly Ile Ile Asp Ala	2290	2295	2300
Ala Ala Ala Ala Phe Ser Gly Gly Gln Pro Pro Glu Leu Gly Gly Ala	2305	2310	2315
Gly Glu Glu Pro Lys Lys Asp Leu Phe Phe Phe Phe Phe Lys Lys Lys	2325	2330	2335
Leu Asn Ser Ser Leu Val Leu Leu Pro Trp Trp Leu Ala Gly Gly Leu	2340	2345	2350
Thr Ser Gln Glu Glu Ala Trp Thr Thr Val Arg Arg Ala Leu Leu Leu	2355	2360	2365
Met Leu Ser Ser Asn Val Val Val Val Val Pro Leu Asp Asp Lys Ser	2370	2375	2380
Ser Tyr Gly Asn Asn Val Ser Val Val Glu Gln Ser Ala Ala Ala Ala	2385	2390	2395
Ala Val Leu Leu Phe His Gly Gly Arg Gly Tyr Tyr Phe Met Met Asp	2405	2410	2415
Glu Tyr Tyr Arg Ser Cys Cys Trp Trp Ser Gly Trp Trp Phe Asn Asn	2420	2425	2430
Gln Cys Cys Leu Leu Cys Cys His Arg Arg Arg Arg Arg Arg His Ala	2435	2440	2445
Ala Thr Gly Gly Leu Ile Leu Leu Trp Asn Gln Gln Arg Ser Ser Ser	2450	2455	2460
Lys Leu Leu Leu Leu Leu Gln Arg Arg Gly Val Pro Pro Ala Leu Pro	2465	2470	2475
Pro Asn Pro Pro Gly Trp Trp Ile Gln Gln Gln Gln Gln Leu Thr Leu	2485	2490	2495
Leu Glu Ala Pro Pro Asn Ala Ala Pro Phe Met Met Lys Lys Leu Leu	2500	2505	2510
Ser Ile Ile Ile Ile Ile Pro Ser Cys Cys Ser Ala Ala Ala Ser Val	2515	2520	2525
Val His Val Gln Gln Arg Pro Pro Ser Leu Ala Ala Ala Ala Gly	2530	2535	2540
Ile Ile Pro Ser Ile Ile Leu Pro Pro Leu Leu Arg Gly Lys Lys Pro	2545	2550	2555
Ala Phe Phe Phe Phe Phe Gly Met Met Pro Met Ala Ala Leu His His			

2565																2570				2575			
Gln	Glu	Ser	Ser	Arg	Gly	Asn	Asn	Leu	Cys	Cys	Cys	Cys	Cys	Cys	Gly								
2580				2585				2590															
Ser	Ser	Cys	Thr	Thr	Leu	Trp	Lys	Lys	Glu	Asn	Trp	Trp	Ala	Gly	Gly								
2595				2600				2605															
Ser	Ala	Asn	Asn	Asn	Asn	Asn	Lys	Thr	Thr	Gly	Ser	Ser	Gly	Arg	Gly								
2610				2615				2620															
Gly	Leu	Asn	Asn	Val	Gly	Gln	Gln	Asp	Ser	Leu	Leu	Leu	Leu	Ser	Cys								
2625				2630				2635				264											
Ile	Ile	Arg	Thr	Asp	Asp	Cys	Gly	Gly	Trp	Ile	Val	Val	Thr	Ala	Arg								
2645				2650				2655															
Arg	Ala	Phe	Phe	Phe	Phe	Phe	Arg	Arg	Glu	Glu	Trp	Thr	Thr	Gly	Val								
2660				2665				2670															
Ala	Ala	Leu	Gln	Gly	Gly	Pro	Gln	Gln	Leu	Arg	Trp	Trp	Trp	Trp	Trp								
2675				2680				2685															
His	Glu	Glu	Trp	Leu	Cys	Cys	Ser	Trp	Lys	Lys	Arg	Val	Val	Pro	Gly								
2690				2695				2700															
Gly	Val	Ala	Ala	Ala	Ala	Ala	Glu	Ala	Gly	Gly	Tyr	Tyr	Ala	Ala	Cys								
2705				2710				2715				272											
Ala	Ala	Arg	Lys	Gly	Val	Lys	Lys	Ile	Tyr	Tyr	Tyr	Tyr	Tyr	Trp	Lys								
2725				2730				2735															
Arg	Arg	Ala	Met	Met	Lys	Pro	Met	Met	Cys	Ala	Lys	Lys	Trp	Asp	Asp								
2740				2745				2750															
Asn	Ile	Ile	Ile	Ile	Ile	Ile	Phe	Lys	Lys	Gln	Asn	Ser	Thr	Ala	Ala								
2755				2760				2765															
Glu	Pro	Pro	Glu	Met	Pro	Phe	Cys	Cys	Cys	Cys	Val	Thr	Leu	Leu	Glu								
2770				2775				2780															
Ser	Ser	Ser	Val	Ile	Ile	Ser	Gln	Arg	Arg	Glu	Arg	Thr	Thr	Glu	Ser								
2785				2790				2795				280											
Ser	Ser	Ser	Ser	Tyr	Cys	Cys	Lys	Asn	Asn	Leu	Ala	Cys	Cys	Gly	Gln								
2805				2810				2815															
Gln	Ser	Val	Val	Lys	Val	Leu	Leu	Leu	Leu	Leu	Pro	Tyr	Tyr	Ala	Arg								
2820				2825				2830															
Cys	Cys	Leu	Arg	Asn	Asn	Glu	Leu	Leu	Pro	Lys	Glu	Glu	Leu	Ala	Glu								
2835				2840				2845															
Glu	Glu	Glu	Gln	Ser	Ser	Asn	Pro	Leu	Leu	Gln	Glu	Glu	Pro	Leu	Met								
2850				2855				2860															
Met	Met	Tyr	Tyr	Tyr	Val	Trp	Trp	Trp	Trp	Trp	Pro	Gln	Gln	Gln	Ser								
2865				2870				2875				288											
His	His	Thr	Val	Asn	Asn	Asn	Ile	Pro	Pro	Ser	Arg	Arg	Met	Met	Met								
2885				2890				2895															
Met	Met	Arg	Pro	Pro	Trp	Lys	Ser	Ser	Pro	Trp	Arg	Arg	Asp	Val	Val								
2900				2905				2910															
Pro	Pro	Asn	Asn	Gly	His	Ala	Ala	Ala	Ala	Val	Leu	Arg	Arg	Asp	Lys								
2915				2920				2925															
Gly	Gly	Pro	Gly	Gly	Lys	Arg	Pro	Pro	Glu	Glu	Arg	Arg	Glu	Glu	Glu								
2930				2935				2940															
Glu	Glu	Lys	Ile	Thr	Ser	Trp	Phe	Phe	Gln	Thr	Pro	Pro	Arg	Thr	Trp								
2945				2950				2955				296											
Trp	Trp	Trp	Trp	Tyr	Cys	Cys	Leu	Leu	Cys	Cys	Gln	Lys	Pro	Pro	Gly								
2965				2970				2975															

Ser	Ser	Gly	Glu	His	His	Met	Val	Val	Val	Val	Leu	Leu	Lys	Lys	Leu
			2980						2985					2990	
Thr	Tyr	Tyr	Met	Gly	Gly	Gly	Arg	Arg	Val	Thr	Arg	Arg	Gly	Asn	Asn
			2995					3000					3005		
Asn	Asn	Asn	His	Asn	Asn	Leu	Leu	Leu	Gln	Gln	Arg	Arg	Val	Arg	Arg
			3010				3015					3020			
Lys	Leu	Leu	Thr	Arg	Ala	Ala	Ala	Ala	Ala	Asp	Pro	Pro	Ser	Gly	Asn
			3025			3030					3035				304
Asn	Gly	Arg	Ser	Ser	Lys	Val	Val	Gln	Gln	Val	Val	Cys	Ser	Ala	Ala
				3045					3050					3055	
Ala	Ala	Thr	Trp	Pro	Pro	Glu	Lys	Asn	Asn	Gln	Thr	Thr	Ala	Gln	Arg
			3060						3065					3070	
Arg	Glu	Phe	Ile	Ile	Lys	Ser	Ser	Ser	Ser	Ser	Lys	Ser	Cys	Cys	Pro
			3075				3080						3085		
Leu	Leu	Ala	Tyr	Leu	Leu	Arg	Thr	Arg	Arg	Ser	Gly	Gly	Thr	Ala	Asn
			3090				3095					3100			
Asn	Asn	Asn	Asn	Ala	Val	Val	Arg	Pro	Lys	Lys	Ser	Gly	Asn	Asn	Val
			3105				3110				3115				312
Asp	Asp	Arg	Lys	Glu	Glu	Cys	Thr	Asn	Asn	Asn	Asn	Lys	Ala	Gly	Gly
				3125					3130					3135	
Arg	Thr	Cys	Cys	Val	Gln	Gln	Trp	Gly	Gly	Arg	Glu	Lys	Lys	Ala	Val
			3140						3145					3150	
Val	Val	Val	Val	Val	Trp	Glu	Glu	Gln	Arg	Arg	Ser	Arg	Ala	Ala	Met
			3155					3160					3165		
Val	Tyr	Tyr	Gly	Trp	Trp	Ala	Arg	Tyr	Tyr	Tyr	Tyr	Tyr	Glu	Phe	Phe
			3170				3175					3180			
Gly	Pro	Gly	Gly	Ser	Met	Met	Asp	His	His	Gly	Phe	Gln	Gln	Lys	Thr
			3185			3190					3195				320
Gln	Gln	Gln	Gln	Glu	Glu	Glu	Glu	Glu	Gly	Ile	Ile	Leu	Thr	Thr	Thr
				3205					3210					3215	
Asp	Asp	Val	Ile	Arg	Arg	Pro	Gly	Gly	Gly	Gly	Gly	Asn	Gly	Trp	Trp
			3220					3225					3230		
Val	Asp	Asp	Tyr	Ala	Asp	Asp	His	Arg	Trp	Trp	Gly	Thr	Thr	Arg	Ile
			3235				3240						3245		
Thr	Thr	Thr	Thr	Ala	Asp	Asp	Arg	Arg	Ser	Ser	Asn	Tyr	Tyr	Glu	
			3250			3255					3260				
Pro	Thr	Thr	Thr	Lys	Asn	Asn	Asn	Trp	His	Lys	Lys	Val	Met	Glu	
			3265			3270				3275				328	